

## Biology- not Chronology-driven Treatment of Breast Cancer in the Elderly

a report by

**Matti S Aapro**

Executive Director, International Society for Geriatric Oncology (SIOG)

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The European Breast Cancer Conference (EBCC) was recently held in Berlin. Among the many topics discussed, treatment of the ageing breast cancer patient was highlighted during an EuropaDonna teaching lecture, which is summarised here.

Breast cancer is the most common cancer site in women, with 1.15 million new cases worldwide each year, of which 361,000 (27.3% of all cancers in females) are in Europe and 230,000 (31.3%) in Northern America. This means that half, if not more, of these patients are in other parts of the world, a fact recognised by the World Health Organization (WHO), which has put cancer among its health priorities on a global scale. In 2002, 411,000 women died of breast cancer worldwide, and most of these were aged 65 years or older. This is explained by the following figures. The crude incidence of breast cancer in Northern America in comparison with North and Western Europe is 141.9 and 130.0 per 100,000 females per year, respectively. Breast-cancer-related mortality is 29.8 and 41.0 per 100,000 females, respectively. For those aged 65 years and older, crude incidence rates are 432.7 per 100,000 females in Northern America and 295.0 per 100,000 in Northern and Western Europe; corresponding breast cancer mortality figures are 121.2 and 135.0 per 100,000 females, respectively. Similar incidence rates and mortality figures are found in South America (Argentina and Uruguay), New Zealand and Australia, and in Central/Eastern Europe.

With increasing age, patients will suffer from ailments related both to senescence and to cancer. Many will need the expertise of the geriatrician and of the oncologist, who will participate in specific case discussions to look at social and medical issues that will affect the treatment plan (with surgery, radiation and drug therapy, rehabilitation and supportive and palliative care questions often intertwined). The wishes of the patient are key in this discussion.<sup>1</sup> The variable reality of family or community support must also be taken into consideration, as this differs so widely among cultures; the ways in which these cultures are changing are also

important, especially as the modern world moves very fast – faster than most elderly (and not so elderly) people can apprehend.<sup>2</sup>

It is therefore interesting to note that there are data that confirm that, when faced with the disease, individuals on both sides of the Atlantic react in a similar way, even when they are 'senior citizens'. Indeed, a view often held in Europe is that older Europeans are less willing than older Americans to undertake chemotherapy.<sup>3</sup> Three hundred and twenty French and American outpatients aged 70 years and older (29% were 80 years or older) with and without cancer were interviewed (and 61% responded) via anonymous questionnaires. The patients were given two scenarios to evaluate: a strong chemotherapy (platinum/taxane combination-like) and a milder chemotherapy (weekly vinorelbine-like). The options were to refuse chemotherapy or to accept it for a threshold chance of cure, life prolongation or symptom relief. The questionnaire contained items assessing the functional status, education and self-rated health and depression of the respondents. The French non-cancer patients (34% accepted) were less willing to accept the strong chemotherapy than French cancer patients (77.8% accepted), American non-cancer patients (73.8% accepted) and American cancer patients (70.5% accepted;  $p < 0.001$  for each pair). This was also true for the moderate chemotherapy, with acceptance rates of 67.9 versus 100, 95.2 and 88.5%, respectively ( $p < 0.001$  for each pair). While outpatient age and sex did not correlate with response, self-rated health, cancer status and nationality did.

The International Society of Geriatric Oncology (SIOG) has created a task force to assess the available evidence on breast cancer in elderly individuals, and to provide evidence-based recommendations for the diagnosis and treatment of breast cancer in such individuals. A review of the published work was performed via the results of a search on Medline for English-language articles published between 1990 and 2007 and of abstracts from key international conferences. Recommendations on the topics of screening, surgery, radiotherapy, (neo)adjuvant hormone treatment and chemotherapy and metastatic disease are found in these recommendations.<sup>4</sup> Oncologists are now learning to take into account the physiological age of their patient, which is the reflection of a normal and sometimes abnormally accelerated loss of body reserves, certainly related to chronological age but not precisely dictated by it. Understanding the biology of breast cancer will allow clinicians to optimally adapt the treatment of the elderly patient, considering that cancer treatments should not be synonymous with undue hardship imposed on patients who would in any case die from another competing cause of mortality.<sup>5,6</sup>

A question addressed during one of the plenary sessions at the EBCC was related to post-operative radiotherapy following breast-conserving surgery (BCS). Combined with appropriate systemic therapy, post-operative



Matti S Aapro is Executive Director of the International Society for Geriatric Oncology (SIOG) and Past President of the Multinational Association for Supportive Care in Cancer (MASCC). In addition to being a Member of the Board of the European Organisation for Research and Treatment of Cancer (EORTC), he chairs the EORTC Cancer in the Elderly Task Force. Dr Aapro is also Dean of the Multidisciplinary Oncology Institute in Genolier, Editor in Chief of *Critical Reviews in Oncology/Hematology*

and [www.cancerworld.org](http://www.cancerworld.org), Associate Editor of *Annals of Oncology* and Section Editor for *The Oncologist*. He has authored more than 180 publications and his major interests are new drug development, breast cancer, cancer in the elderly and supportive care.

E: [maapro@genolier.net](mailto:maapro@genolier.net)

radiotherapy has been shown to achieve an absolute risk reduction in five-year local recurrence from 26 to 7%, and a 15-year absolute breast cancer mortality risk reduction from 35.9 to 30.5%. Despite these benefits, elderly patients continue to receive radiotherapy less frequently after BCS than younger patients. A number of randomised trials usually limited to an upper age limit of 70 years show a statistically significant reduction in risk of local recurrence from post-operative breast irradiation, but no impact on overall survival. Some trials have found age to be a factor that predicts for a lower risk of local recurrence after whole-breast irradiation compared with conservative surgery alone. Several studies have specifically evaluated the benefits of radiotherapy in the elderly. All large studies have shown a relative decrease in local relapse rate. However, the absolute incidence of relapse, as well as the absolute benefit from radiotherapy, tended to be low, and data on overall survival were generally absent, with the exception of one trial.<sup>4</sup>

Some have concluded that radiotherapy may be avoided in low-risk older patients, while others have suggested that it may offer benefits in terms of slight reductions in local relapse rates and improvements in overall survival, and maintain that post-operative breast irradiation should be considered in all patients undergoing BCS, irrespective of age. For women aged >70 years with a low risk of recurrence (e.g. small tumours  $\leq 2$ cm, clear margins, axillary node-negative, hormone-receptor-positive with plans to receive

endocrine therapy), the absolute reductions in local recurrence tend to be slight, and mortality is usually associated with non-breast-cancer-related conditions. The use of radiotherapy in such patients should therefore depend on a multidimensional evaluation, including the absolute benefit of radiotherapy, co-morbidity, life expectancy and patient preference.

However, biases prevail in the treatment of breast cancer in the elderly; for example, although adjuvant breast cancer chemotherapy is yet to be accepted and codified in the elderly, there is a remarkable exercise of schizophrenic thinking about chemotherapy, with lymphoma experts feeling that anthracyclines are part of curative treatment in the elderly while breast cancer experts debate the potential for cardiac insufficiency related to these drugs. Women over 70 years of age who are treated with chemotherapy for metastatic disease derive similar benefits to their younger counterparts. The use of chemotherapy should thus always be considered in hormone-receptor-negative or hormone-refractory patients. Preference should be given to chemotherapeutic agents with 'safer' profiles such as weekly taxane regimens, newer, less cardiotoxic anthracycline formulations, capecitabine, gemcitabine and vinorelbine. Treatment proposals should be made on the basis of objective evidence and evidence-based reasoning;<sup>7</sup> the subjective and sometimes highly emotional discussions are understandably part of the patient's reactions. ■

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## Events Diary 2009

### 13–15 February

European School of Haematology Conference on Haematological Aspects of Auto-immune Diseases  
Mandelieu, France  
[www.esh.org](http://www.esh.org)

### 6–10 March

21st European Congress of Radiology  
Vienna, Austria  
[www.myesr.org](http://www.myesr.org)

### 21–26 March

Third European Oncology Nursing Society – European School of Oncology Masterclass in Oncology Nursing  
Sintra, Portugal  
[www.cancerworld.org](http://www.cancerworld.org)

### 27–28 March

European Organisation for Research and Treatment of Cancer and the European Association of Neuro-Oncology Conference 2009  
Budapest, Hungary  
[www.eortc.be](http://www.eortc.be)

### 29 March – 1 April

35th Annual Meeting of the European Group for Blood and Marrow Transplantation  
Göteborg, Sweden  
[www.ebmt.org](http://www.ebmt.org)

### 26 May – 2 June

American Society of Clinical Oncology Annual Meeting  
Orlando, FL, US  
[www.asco.org](http://www.asco.org)

### 25–27 June

Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology 2009 International Symposium  
Rome, Italy  
[www.mascc.org](http://www.mascc.org)

### 4–6 September

Third Annual Meeting of the International Liver Cancer Association  
Milan, Italy  
[www.ilca-online.org](http://www.ilca-online.org)

### 20–24 September

European Cancer Organisation 15 and 34th European Society of Medical Oncology Multidisciplinary Congress  
Berlin, Germany  
[www.ecco-org.eu](http://www.ecco-org.eu)

### 24–25 September

The European Association for Cancer Research Special Conference on Inflammation and Cancer  
Berlin, Germany  
[www.eacr.org](http://www.eacr.org)

### 15–17 October

10th International Society of Geriatric Oncology Meeting  
Berlin, Germany  
[www.cancerworld.org](http://www.cancerworld.org)

### 5–8 December

2009 American Society of Hematology Annual Meeting  
New Orleans, LA, US  
[www.hematology.org](http://www.hematology.org)